Journal of Molecular Structure 1248 (2022) 131449

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstr

Synthesis, characterization and application of α-Ca_3 $(PO_4)_2$ as a heterogeneous catalyst for the synthesis of 2.3-diphenylquinoxaline derivatives and knoevenagel condensation under green conditions

Haddou Anahmadi[a], Majda Fathi[b], Fatima El hajri[a], Zakaria Benzekri[a,*], Sarra Sibous[a], Brahim Chafik El Idrissi[b], Mohamed Salahdine El youbi[a], Abdelaziz Souizi[a], Said Boukhris[a]

[a] *Laboratory of Organic Chemistry, Catalysis and Environment, Department of Chemistry, Faculty of Sciences, Ibn Tofail University PO Box 133, Kenitra 14000, Morocco*

[b] *Advanced Materials and Process Engineering, Faculty of Sciences, Ibn Tofaïl University, PO Box 133, Kenitra 14000, Morocco*

ARTICLE INFO

Article history:
Received 3 June 2021
Revised 6 August 2021
Accepted 4 September 2021
Available online 6 September 2021

Keywords:
Green chemistry
Heterogeneous catalyst
Tricalcic phosphate α-TCP
Knoevenagel condensation
2.3-diphenylquinoxalines

ABSTRACT

Green chemistry is now paramount in modern life and industrial sector. It has become a research priority and a scientific challenge. In this study, alpha-tricalcic phosphate was prepared as a green catalytic medium. This medium has been characterized by various techniques such as X-ray diffraction (XRD), Fourier Transformed Infrared Spectroscopy (FT-IR), Scanning Electron Microscope (SEM) in combination with dispersive energy X-ray microanalysis (EDX). Furthermore, we studied the catalytic performance of α-Ca_3 $(PO_4)_2$ on knoevenagel condensation and the synthesis of 2.3-dipphennylquinoxaline derivatives. These methodologies present several beneficial ones such as mild conditions, increased reaction speed, excellent yields, ease of implementation and insulation of products. In addition, this new phosphate-based catalytic medium can be recycled several times without losing either their activity or selectivity.

1. Introduction

Calcium phosphates are widely used in different areas, like the phosphate fertilizer manufacturing industry [1]. In addition, calcium phosphates have electronic properties, are widely used in the design of fluorescent lamps [2] and laser materials [3]. Similarly, they are also used in chromatography for the separation and purification of organic molecules [4–5].

Therefore, apatitic calcium phosphates having a great activity in the biomaterials field. Indeed, thanks to their chemical composition close to the mineral phase of bone tissues, their biocompatibility and bio-activity properties make them usable in various forms: bone substitutes, active-principle release system, ceramics and cements [6–9]. Also, calcium phosphates are widely used in organic synthesis in shaves of their diversity of properties.

One of their important applications is their uses as catalysts in organic synthesis [10–13]. The Knoevenagel condensation is discovered by Knoevenagel [14] who caused benzaldehyde to react with ethyl acetoacetate to form ethyl benzylidene acetoacetate [15].

This reaction is one of the most common for the formation of functionalized alkynes in the presence of a weak base. The reaction is also carried out by various heterogeneous catalysts including natural phosphate and trisodium phosphate (TSP) [16].

The synthesis of the activated alkenes is performed under mild conditions using natural phosphate alone, doped by potassium fluoride or modified by sodium nitrate in methanol at room temperature [17]. We represent the different methods of alkenes synthesis (Knoevenagel condensation) by the use of different varieties of catalysts [18–22]. The quinoxalins are bicyclic heterocycles compounds containing a benzene nucleus fused to a pyrazine ring [23–25].

The chemistry of quinoxalins has recently undergone considerable development, due to the evidence of applications, of several quinoxalins derivatives in various fields, be it in pharmaceutical chemistry [26–28], or in agrochemicals [29,30]. The studies have shown that quinoxalins exhibit biological activities such as anticancer, antimicrobial, antibiotic, antiviral, anti-inflammatory, antibacterial and antiproliferative [31–35]. Also, they are used as dyes, luminescent materials, semi-conductors and corrosion inhibitors [36–39]. But before exposing our own synthesis methods, it seemed appropriate to cite the different procedures allowing access to quinoxalins and derivatives [40–44]. In this context, the heterogeneous catalysis is one of the pillars of clean chemistry. Therefore, we continued our axis of research using the α-$Ca_3(PO_4)_2$ as a heterogeneous catalyst for the synthesis of alkene and 2.3-diphenylquinoxalines derivatives.

---

[*] Corresponding author.
E-mail address: zakariachimist2014@hotmail.com (Z. Benzekri).

https://doi.org/10.1016/j.molstruc.2021.131449

2. Experimental

2.1. Materials and equipment

All chemicals and solvents used were obtained from Sigma Aldrich and Merck without any additional purification. The X-ray diffraction analysis of our catalytic medium was performed under ambient pressure and temperature conditions, performed on a PANalytical X'Pert 3 Powder diffractometer using the source of the Cu K-radiation (1.54178) source generated at 45 KV and 40 mA. The infrared absorption spectrum of our catalyst was recorded on a VERTEX 70v DTGS type device. The sample was analyzed as a potassium bromide (KBr) pellet. The analysis is carried out at room temperature on a spectral domain of 400 cm^{-1} to 4000 cm^{-1}. The surface morphology of the used catalyst was determined using a type scanning electron microscopy (TESCAN-VEGA3) equipped with a complete EDAX-type microanalysis detector to analyze the chemical composition of a sample. The progression and follow-up of all reactions were monitored by thin-film aluminum chromatography covered with silica gel 60 F254 (0.2 mm thick) were carried out on Merck plates. The revelation was carried out by observation under ultraviolet lamp (UV 254 nm). The melting points of the synthesized compounds were determined using a previously calibrated kofler bench. The structural analysis of the synthesized compounds was carried out by the Nuclear Magnetic Resonance (NMR) of proton ^{1}H and carbon ^{13}C. The NMR ^{1}H and ^{13}C spectra were recorded on a BRUKER DPX 250 spectrometer operating at frequencies of 300 and 75 MHz, respectively. The chemical movements (δ) are expressed in part per million (ppm) compared to the tetramethylsilane (TMS) signal used as a reference.

2.2. General protocol of Knoevenagel condensation

In a beaker of 50 ml added aromatic aldehyde (**1**) **(1 mmole),** malononitrile **(1 mmole)**, ethyl cyanoacetate or methyl cyanoacetate (**2**) with 2.56 mg of α-$Ca_3(PO_4)_2$ as a catalyst in 2 ml of ethanol. The reaction mixture was stirred at room temperature for a time (Table 5). The reaction was followed by TLC using n-hexane/EtOAc (5:1) as an eluent. After the reaction is completed, the resulting crude product is dissolved in CH_2Cl_2. The α-$Ca_3(PO_4)_2$ was then recovered by a simple filtration. The pure products were obtained after recrystallization in ethanol.

2.3. General procedure of the synthesis of 2.3-diphenylquinoxalines derivatives

1.2-diamine **4** (**1 mmole**) and benzile **2** (**1 mmole**) were mixed in 2 ml of ethanol in the presence of α-$Ca_3(PO_4)_2$ (2.56 mg) as a catalyst. The reaction mixture was stirred at room temperature for an illustrious time in Table 6. When the reaction is completed [TLC control (elected: Ethyl acetate: n-Hexane (1:9)))]. Then, Dichloromethane was added to the mixture to recover the catalyst by simple filtration. After removing the CH_2Cl_2 by simply evaporation of the solvent. The obtained crude solid is well recrystallized in EtOH.

2.4. Spectroscopic characterization data

2-(4-chlorophenylmethylene) malononitrile **(3a)**: Colorless solid, mp 160–162 °C; **IR** (KBr, cm^{-1}): 2222 (CN), 1585 ($C = C$).**^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.49 (s, 1H, C=CH), 7.92 (d, 2H, $J = 8.7$ Hz), 7.67 (d, 2H, $J = 8.7$ Hz). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 160.5, 139.5, 132.5, 131.6, 130.1, 114.4, 113.4, 82.7.

2-(phenylmethylene) malononitrile **(3b)**: Colorless solid, mp 80–81 °C; **IR** (KBr, cm^{-1}): 2225 (CN), 1560 ($C = C$).**^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.50 (s, 1H, C=CH), 7.59 (d, 2H, $J = 7.7$ Hz, ArH), 7.57–7.70 (m, 3H, ArH). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 155.7, 134.8, 131.7, 131.6, 130.9, 129.9, 114.6, 113.5, 82.0.

2-(p-tolylmethylene) malononitrile **(3c)**: White solid, mp 118–119 °C; **IR** (KBr, cm^{-1}): 2222 (CN), 1593 ($C = C$).^{1}H NMR (300 MHz, DMSO–d_6) δppm 8.39 (s, 1H, C=CH), 7.82 (d, $J = 8.5$ Hz, 2H), 7.38 (d, $J = 8.5$ Hz, 2H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, DMSO–d_6) δppm 161.6, 146.1, 131.1, 130.5, 129.1, 114.8, 113.8, 80.3, 21.5.

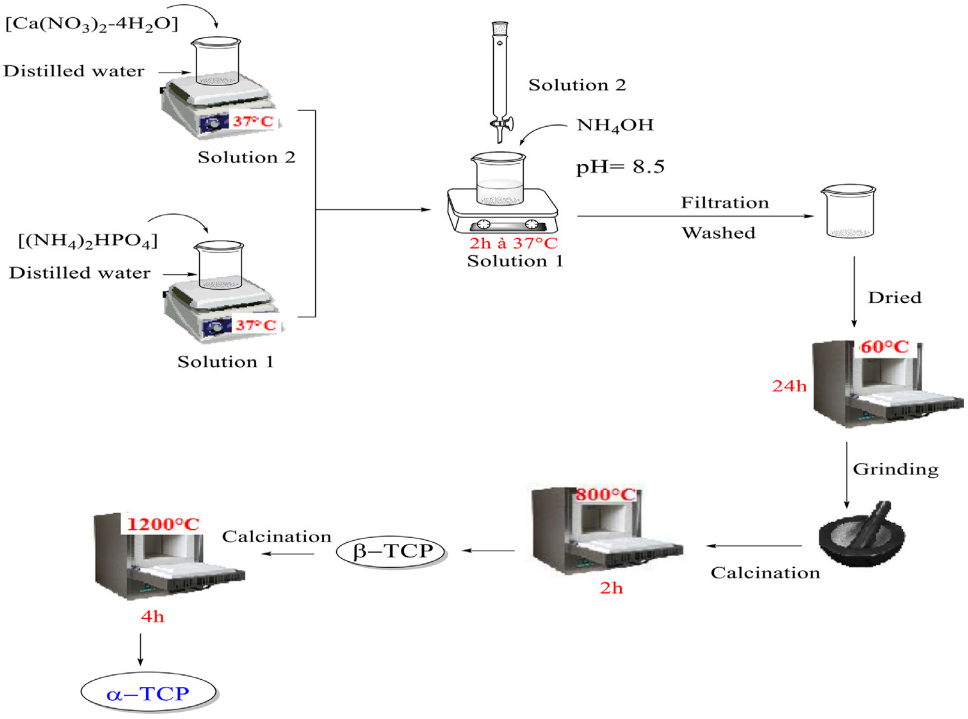


Fig. 1. Catalyst preparation steps α-Ca_3 $(PO_4)_2$.

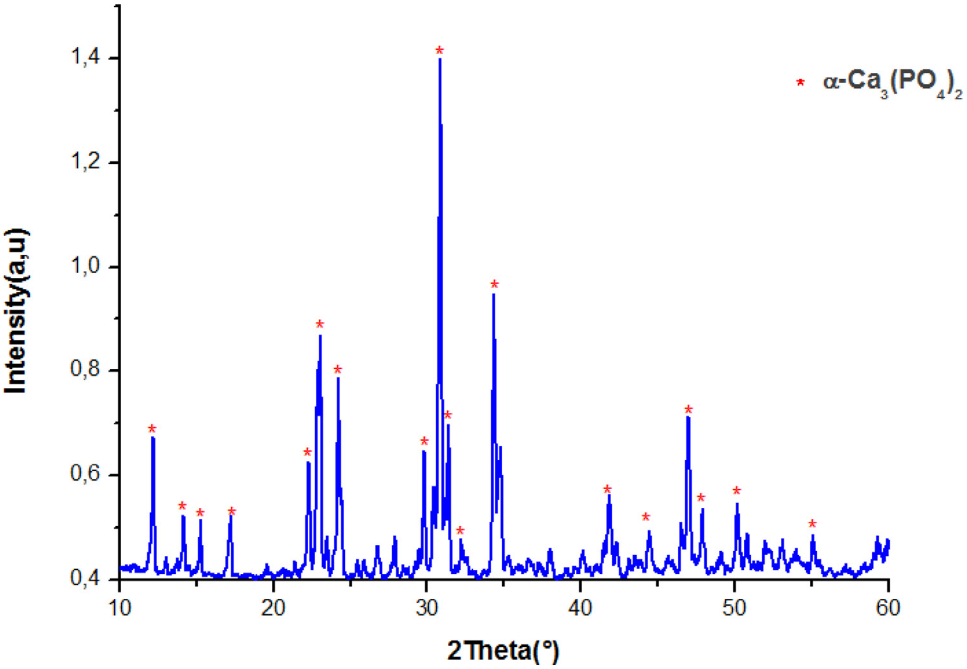


Fig. 2. X-ray diagram of α-$Ca_3(PO_4)_2$.

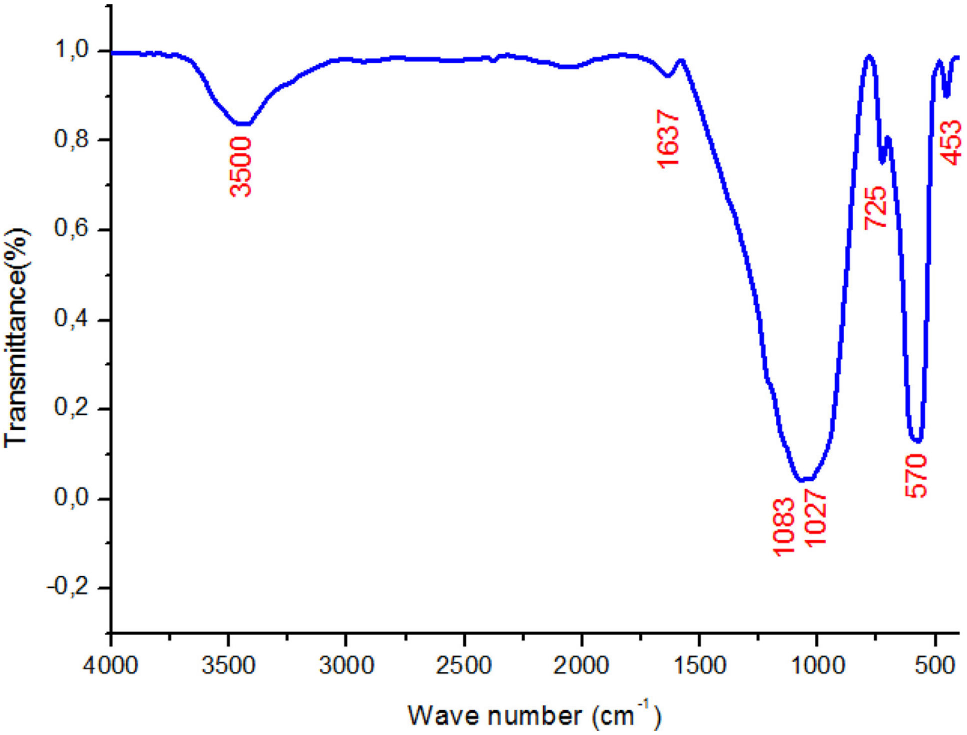


Fig. 3. FT-IR absorption spectrum of α-$Ca_3(PO_4)_2$.

Table 1
Positions and modes of vibration (FT-IR) of α-$Ca_3(PO_4)_2$.

Wave number (cm^{-1})	Functional grouping	Normal modes	Reference
3500	H_2O	Elongation vibrations.	[47]
1637		Deformation in the plane of the water molecule adsorbed on the particles surface.	[47]
1027–1083	P – O	Triple degenerate antisymmetric vibration mode.	[45]
570	P – O	Antisymmetric bending triply degenerte.	[45]
453	P – O	Symmetric bending doubly degenerte.	[45]

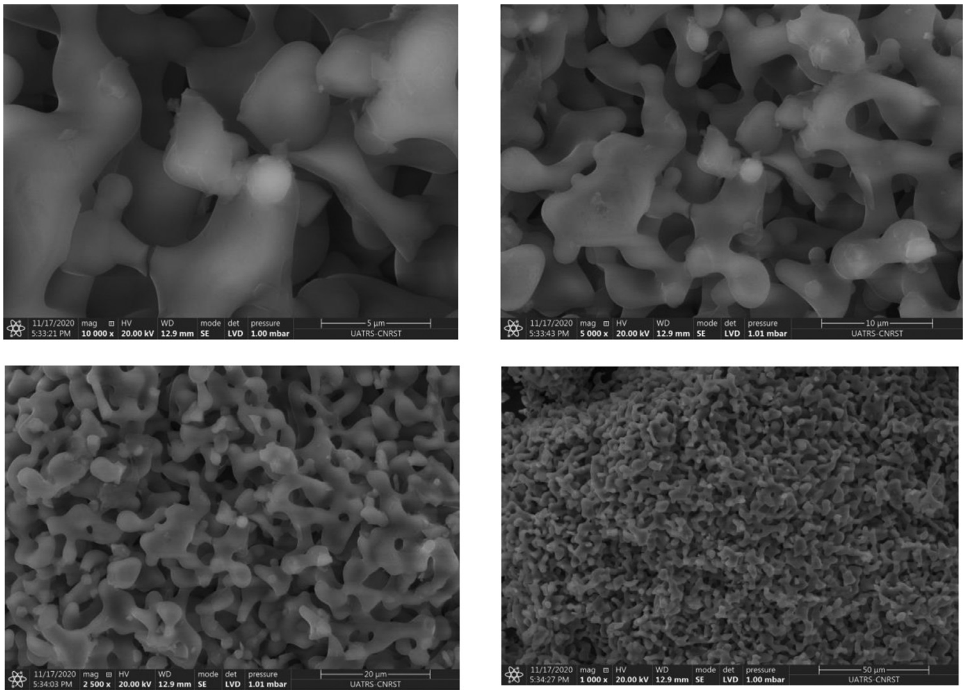


Fig. 4. SEM of α-$Ca_3(PO_4)_2$.

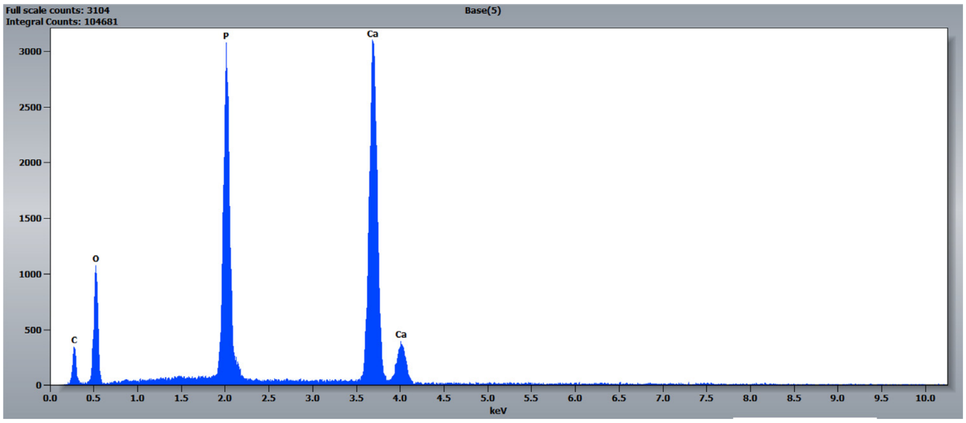


Fig. 5. Spectroscopy of dispersive energy (EDS) of α-$Ca_3(PO_4)_2$.

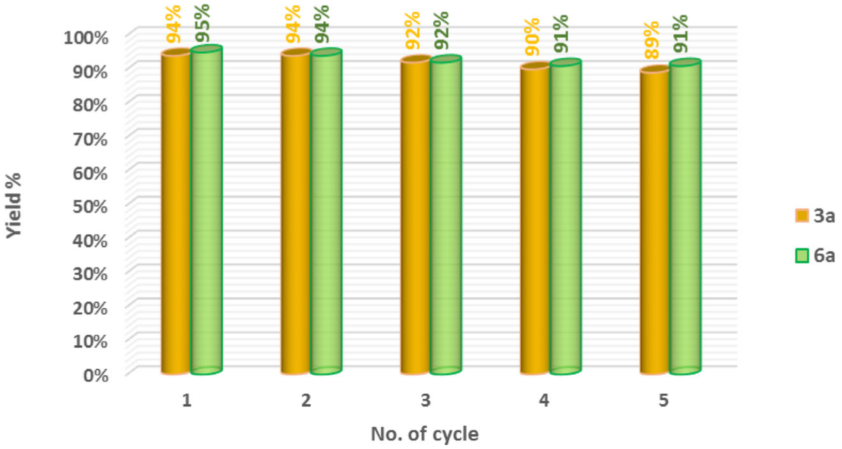
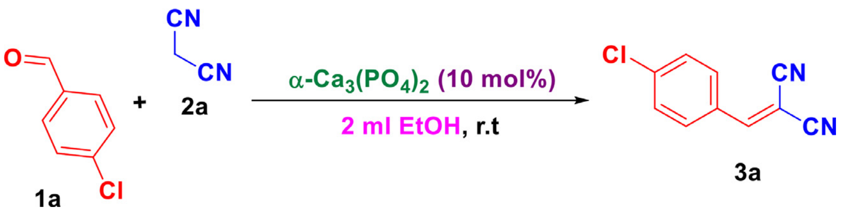
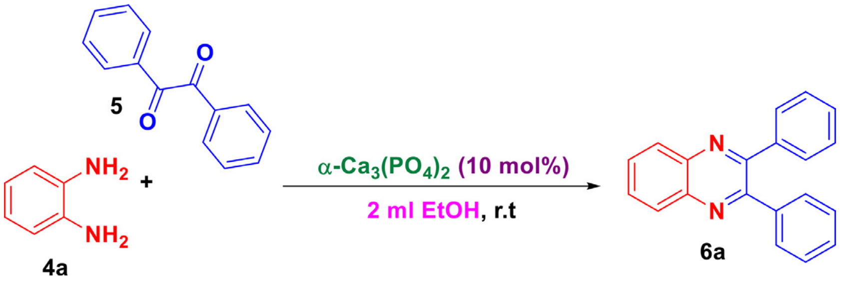


Fig. 6. Long durability of α-$Ca_3(PO_4)_2$ in the formation of products 3a and 6a.



Scheme 1. Model topical: condensation of 4-chlorobenzaldehyde 1a and malononitrile 2a.



Scheme 2. Ideal reaction: condensation of o-phenylenediamine 4a and benzil 5.

Table 2
Catalytic test on model tropical.

Entry	Catalyseur	Time (min)[b]		Yield%[a]	
		3a	6a	**3a**	**6a**
1	No catalyst	60	10	54	47
2	α-$Ca_3(PO_4)_2$	30	10	91	95

[a] Isolated yields.
[b] Determined by TLC.

Table 3
Study of the effect of solvent on model reactions.

Entry	Solvent	Time (min)[b]		Yield(%)[a]	
		3a	6a	3a	6a
1	EtOH	30	10	91	95
2	MeOH	30	12	90	92
3	THF	45	20	86	––
4	CH_3CN	40	15	67	––

[a] Isolated yields.
[b] Determined by TLC.

Table 4
Study of the difference of the mass of the catalyst on the formation of products **3a** and **6a**.

Entry	α-$Ca_3(PO_4)_2$ (mol%)/(mg)	*Yield(%) of 3a*[a]	*Yield(%) of 6a*[a]
1	1/0.32	59	54
2	2/0.64	60	68
3	3/0.96	61	73
4	4/1.28	62	76
5	5/1.60	74	78
6	6/1.92	78	80
7	7/2.24	80	89
8	8/2.56	**94**	**95**
9	9/2.88	94	95
10	10/3.20	91	95
11	20/6.44	86	89

[a] Isolated yields.

***2-(4-nitrophenylmethylene) malononitrile* (3d)**: Yellow solid, mp 161–162 °C; **IR** (KBr, cm^{-1}): 2225 (CN), 1600($C = C$).**^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.67 (s, 1H, C=CH), 8.29 (d, J = 8.7 Hz, 2H), 8.11 (d, J = 8.7 Hz, 2H). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 159.7, 150.1, 137.1, 131.9, 124.8, 114.0, 112.9, 82.4.

***Methyl-3-(4-chlorophenyl)–2-cyanoacrylate* (3e)**: White solid, mp 120–121 °C; **IR** (KBr, cm^{-1}): 2230 (CN), 1720 ($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.38 (s, 1H, C=CH), 8.04 (d, 2H, J = 8.4 Hz, ArH), 7.65 (d, 2H, J = 8.4 Hz, ArH), 3.84 (t, 3H, O–$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 162.5, 154.2, 138.5, 132.5, 130.6, 129.9, 115.8, 103.4, 53.8.

***Methyl-2-cyano-3-phenylacrylate* (3f)**: White solid, mp 84–85 °C; **IR** (KBr, cm^{-1}): 2235 (CN), 1725($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.38 (s, 1H, C=CH), 8.01–8.04 (m, 2H, ArH), 7.54–7.65 (m, 3H, ArH), 3.84 (t, 3H, O-$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 162.8, 155.6, 133.9, 131.7, 131.6, 129.8, 115.0, 102.8, 53.8.

***Methyl-2-cyano-3-(4-nitrophenyl) acrylate* (3 h)**: Yellow solid, mp 172–173 °C; **IR** (KBr, cm^{-1}): 2232 (CN), 1722($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.48 (s, 1H, C=CH), 8.34 (d, 2H, J = 7.1 Hz, ArH), 8.19 (d, 2H, J = 7.1 Hz, ArH), 3.88 (s, 3H, O–$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 162.1, 153.1, 149.8, 137.6, 132.1, 131.0, 124.4, 115.1, 107.0, 53.9.

***Ethyl-3-(4-chlorophenyl)–2-cyanoacrylate* (3i)**: Colorless solid, mp 89–90 °C; **IR** (KBr, cm^{-1}): 2230 (CN), 1725($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.33 (s, 1H, C=CH), 8.00 (d, 2H, J = 8.7 Hz, ArH), 7.61 (d, 2H, J = 8.7 Hz, ArH), 4.29 (q, 2H, J = 7.2 Hz, O–$\underline{CH_2}$–CH_3), 1.28 (t, 3H, J = 7.2 Hz, O–CH_2–$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 162.0, 154.0, 138.5, 132.8, 130.5, 129.8, 115.7, 103.5, 62.9, 14.3.

***Ethyl-2-cyano-3-p-tolylacrylate* (3k)**: White solid, mp 91–92 °C; **IR** (KBr, cm^{-1}): 2235 (CN), 1730($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.05 (s, 1H, C=CH), 7.90 (d, J = 7.2 Hz, 2H), 7.79 (d, J = 7.5 Hz, 2H), 4.34 (q, J = 7.4 Hz, 2H, O–$\underline{CH_2}$–CH_3), 2.37 (s, 3H, O–CH_2–$\underline{CH_3}$), 1.31 (t, J = 7.2 Hz, 3H, Ar-$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 163.0, 155.5, 144.9, 131.4, 130.4, 129.1, 116.2, 101.2, 63.1, 14.3, 21.3.

***Ethyl-2-cyano-3-(4-nitrophenyl) acrylate* (3l)**: Yellow solid, mp 168–169 °C; **IR** (KBr, cm^{-1}): 2230 (CN), 1720 ($C = O$). **^{1}H NMR** (300 MHz, DMSO–d_6) δppm 8.35 (s, 1H, C=CH), 8.02 (d, 2H, J = 8.4 Hz, ArH), 7.62 (d, 2H, J = 8.4 Hz, ArH), 4.29 (q, 2H, J = 7,2 Hz, O–$\underline{CH_2}$–CH_3), 1.28 (t, 3H, J = 7.2 Hz, O–CH_2–$\underline{CH_3}$). **^{13}C NMR** (75 MHz, DMSO–d_6) δppm 162.0, 154.0, 138.4, 132.8, 130.6, 129.9, 115.8, 103.6, 62.9, 14.4.

2,3-diphenylquinoxaline (6a) : White solid, mp 126–128 °C; **IR** (KBr, cm^{-1}): 2971, 1712, 1461, 1299, 767. **^{1}H NMR** (DMSO–d_6, 300 MHz, δ ppm) δ 8.11–8.14 (m, 2H), 7.83–7.86 (m, 2H), 7.43–7.46

Table 5
Knoevenagel condensation via condensation of the various aromatic aldehyde substituted with the active methylene compound catalyzed by α-Ca_3 $(PO_4)_2$.

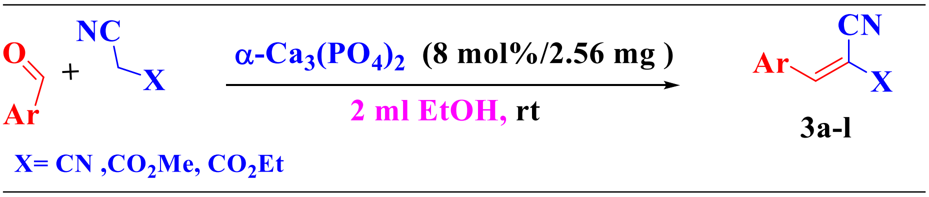
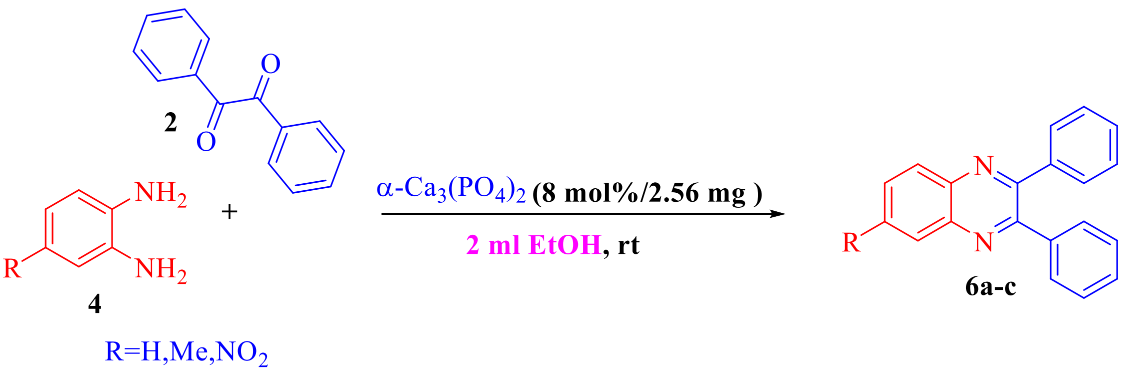
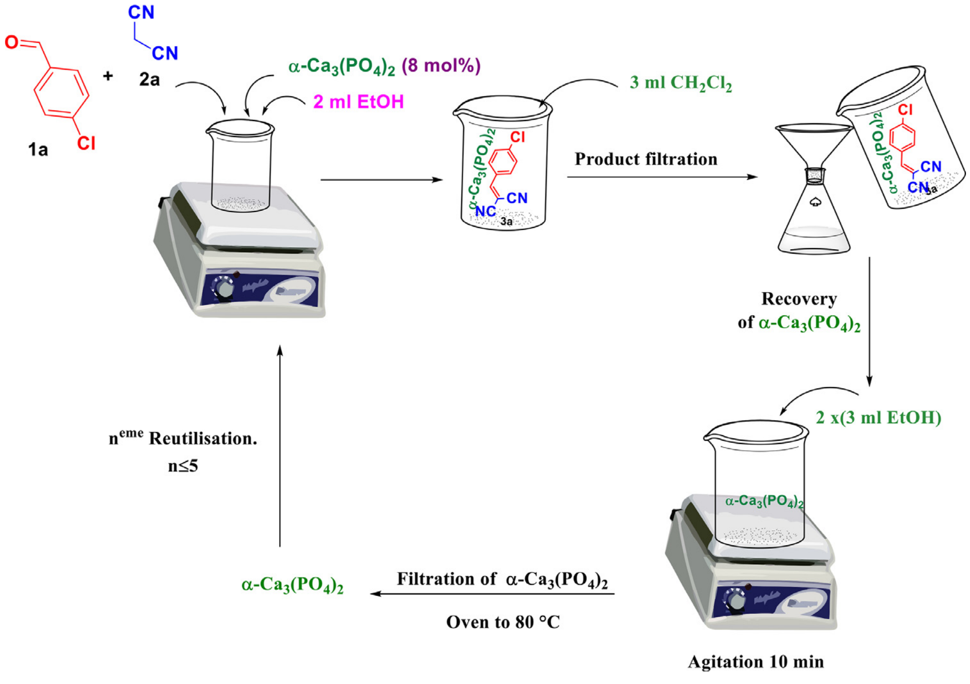


Table 6
Synthesis of 2,3-diphenylquinoxaline between the condensation of various o-phenylenediamine substituted with benzil in the presence of α-Ca_3 $(PO_4)_2$.





Scheme 3. Recycling of α-Ca_3 $(PO_4)_2$ tricalcium phosphate in the formation of product **3a**.

(m, 4H), 7.32–7.37 (m, 6H). **^{13}C NMR** (DMSO–d_6, 75 MHz, δ ppm) δ 153.5, 140.9, 139.2, 132.0, 130.9, 130.2, 129.2, 128.5.

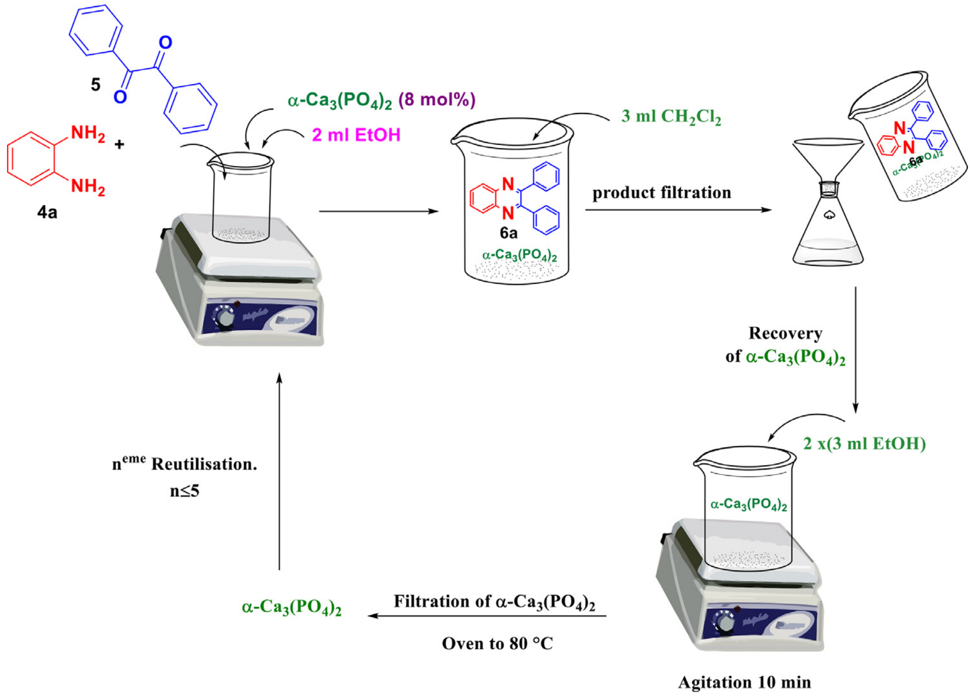
6-methyl-2,3-diphenylquinoxaline (6b) : White solid, mp 122–124 °C; **IR** (KBr, cm^{-1}): 3405, 1623, 1451, 1350, 1063, 759, 697. **^{1}H NMR** (DMSO–d_6, 300 MHz, δ ppm) δ 7.90–7.99 (m, 2H), 7.66–7.69 (m, 2H), 7.44–7.66 (m, 4H), 7.28–7.44 (m, 5H), 2.47 (s, 3H, CH_3). **^{13}C NMR** (DMSO–d_6, 75 MHz, δ ppm) δ 153.3, 141.0, 139.3, 133.0, 130.1, 129.1, 128.8, 127.9, 21.8.

6-Nitro-2,3-diphenylquinoxaline (6c) : Red solid, mp 140–142 °C; **IR** (KBr, cm^{-1}): 3413, 1768, 1526, 1345, 1064, 755. **^{1}H NMR** (DMSO–d_6, 300 MHz, δ ppm) δ 8.85–8.86 (m, 2H), 8.48–8.52 (m, 2H), 8.29–8.32 (m, 4H), 7.32–7.49 (m, 5H). **^{13}C NMR** (DMSO–d_6, 75 MHz, δ ppm) δ 156.5, 143.4, 139.6, 138.4, 136.0, 131.2, 130.2, 129.9, 125.3.

3. Results and discussion

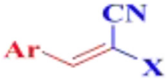
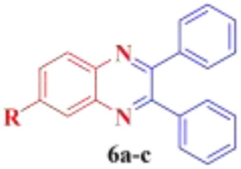
3.1. The preparation and characterization of α-$Ca_3(PO_4)_2$

The reaction conditions for the preparation of **α-$Ca_3(PO_4)_2$** by the slightly modified wet chemical method were initially optimized. The analytical grade calcium nitrate tetrahy-



Scheme 4. Recycling tricalcic phosphate (α-Ca_3 $(PO_4)_2$) in model condensation **6a**.

Table 7
Comparative study between the catalytic performance of α-$Ca_3(PO_4)_2$ with other catalysts.

Entry	Catalyst	Reaction conditions	Yield(%)
	 3a-l	**Condensation of knoevenagel**	
1	Mesoporous Amino-silica	20 mg, EtOH, r.t, 6 h	64–90 [48]
2	HAP- γ- Fe_2O_3	0.025 g, H_2O, 30 °C, 1h	60–99 [49]
3	mpg-C_3N_4-tBu	50 mg, CH_3CN, 70 °C, 2h	48–98 [50]
4	Na-A-PW_9	0.25 mol%, MeOH, r.t, 6h	80–98 [51]
5	R_2 (1MCl-2$NaPO_3$) (2%)	6 mg, 3 mL EtOH,r.t,3–30min	85–98 [52]
6	$(N_2H_5)_2SiF_6$	0.1 mol% ,2 mL EtOH ,r .t , 30–60min	54–98 [53]
7	$CaHPO_4$, $2H_2O$ (DCPD)	10 mg, 3 mL EtOH, r.t, 10 min	84–96 [13]
8	$Na_2Ca(HPO_4)_2$	6 mg, 3 mL EtOH, r.t, 10–65 min	82–97 [58]
9	**α-$Ca_3(PO_4)_2$**	**2.56 mg/8 mol%, 2 mL EtOH, r.t, 30–60 min**	**83–96**
	 6a-c	2,3-diphenylquinoxalins	
10	Fe_3O_4@SiO_2-imid-PMA^n	0,05 g, 5 mL EtOH, r.t, 5–25 min	89–95 [54]
11	RHA-SO_3H	15 mg, Free-solvent, r.t, 5–30 min	90–98 [55]
12	ZrO_2-Al_2O_3	0.03 g, 10 mL EtOH, 80 °C, 20 min	90–91 [56]
13	Co NPs	1 mol%, 5 mL EtOH, r.t, 90 min	88–98 [57]
14	$Ca(H_2PO_4)_2.H_2O$	3 mg, 2 mL EtOH, r.t, 2 min	97–99 [59]
15	**α-$Ca_3(PO_4)_2$**	**2.56 mg/8 mol%, 2 mL EtOH, r.t, 10–15 min**	**90–98**

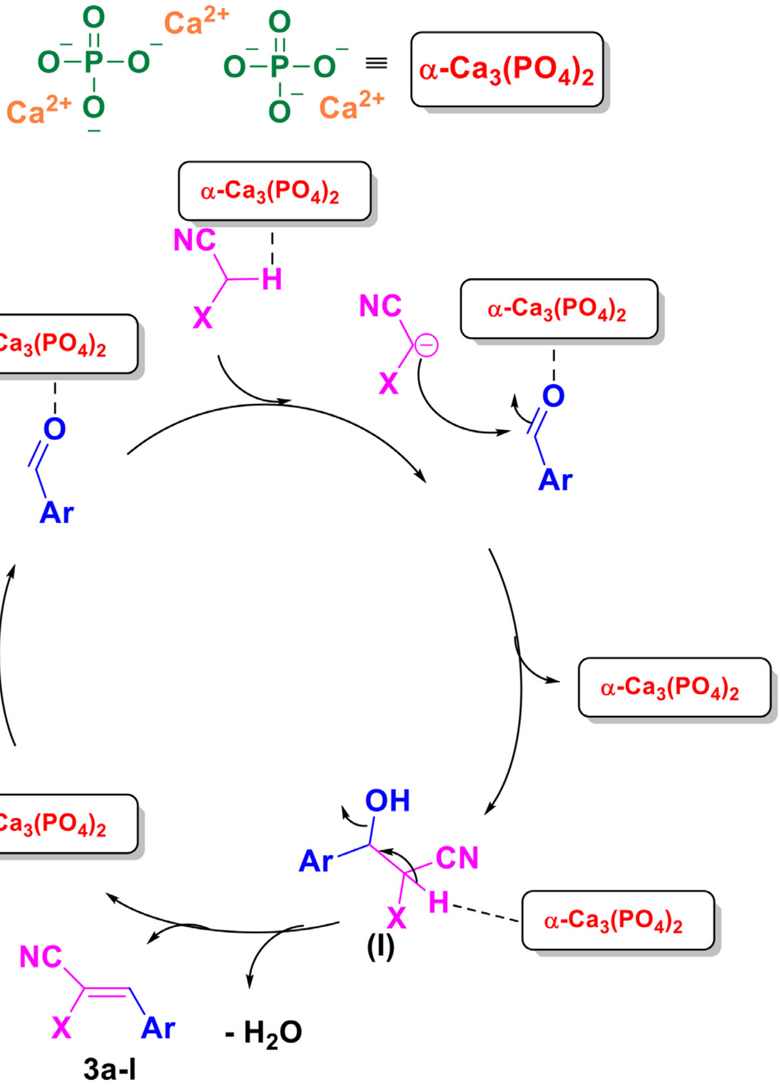
drate [$Ca(NO_3)_2{\cdot}4H_2O$] and diammonium hydrogen phosphate [$(NH_4)_2HPO_4$] were dissolved individually in distilled water preheated at 37 °C. The $Ca(NO_3)_2{\cdot}4H_2O$ solution was added dropwise into $(NH_4)_2HPO_4$ solution under constant stirring to reach the Ca/P molar ratio of 1.50. The temperature of the opaque solution is maintained at 37 °C. The pH was adjusted by the addition of the concentrated ammonium hydroxide (NH_4OH) solution at around 8. The milky solution is stirred for 2 h at 37 °C. The formed precipitates are then filtered out of the mother liquor, washed repeatedly with distilled water to remove NO_3^- and NH_4^+, followed by drying in an air atmosphere at 60 °C for 24 h. The obtained cake after drying was powdered with agate mortar and pestle, and then calcined into alumina crucible at 800 °C for 2 h. The product was determined to be pure β -TCP. Afterwards, the prepared β –TCP was calcined at 1200 °C followed by quenching to room temperature (r.t). The calcination is performed as follows: β –TCP powders are heated from r.t to 1200 °C for 4 h, soaked at 1200 °C for 3 h, followed by quenching, in the furnace, from

1200 °C to r.t for 4 h (Fig. 1). The X-ray diffraction showed the presence of all characteristic peaks at a single phase of α-$Ca_3(PO_4)_2$ (Fig. 2). Their intensities indicate that it has been well crystallized and its crystalline structure is monoclinical with $P2_1/a$ space group (JCPDS 00–009–0348) [45,46]. The crystalline parameters determined using the 'High Score plus' software are a of a = 12,859(2) Å, b = 27,354(2)Å, c = 15,222(3)Å, $\alpha=\gamma=90°$, $\beta=$ 126,35° The FT-IR analysis of the catalytic support allowed us to identify the absorption bands of the different groups characteristic of α-$Ca_3(PO_4)_2$ (Fig. 3). All bands have been listed in Table 1. Moreover, a less intense band at 725 cm^{-1} is corresponding to the P_2O_7 grouping [12]. Based on the scanning electron microscopy (SEM) analysis of our catalytic support, the α-$Ca_3(PO_4)_2$ with different enlargements 5, 10, 20 and 50 µm are shown in Fig. 4. The obtained micrographs showed clearly that the α-$Ca_3(PO_4)_2$ surface had a heterogeneous microstructure is mainly composed of irregular geometry particles in agglomerated form. Furthermore, the surface of these agglomerates is moderately smooth with a low visible porosity. To determine the nature of the elements in the studied sample, a dispersive energy spectroscopy (**EDS**) analysis was performed. From the EDS analysis of our support, showed clearly the presence of the characteristic peaks of the elements Ca, P, O and C (Fig. 5). This results confirmed that the structure of our support is type α-$Ca_3(PO_4)_2$. In addition, no trace of impurity was detected in the EDS spectrum.

3.2. Catalytic performance of α-Ca$_3$(PO$_4$)$_2$ on Knoevenagel condensation and the synthesis of 2.3-diphenylquinoxaline

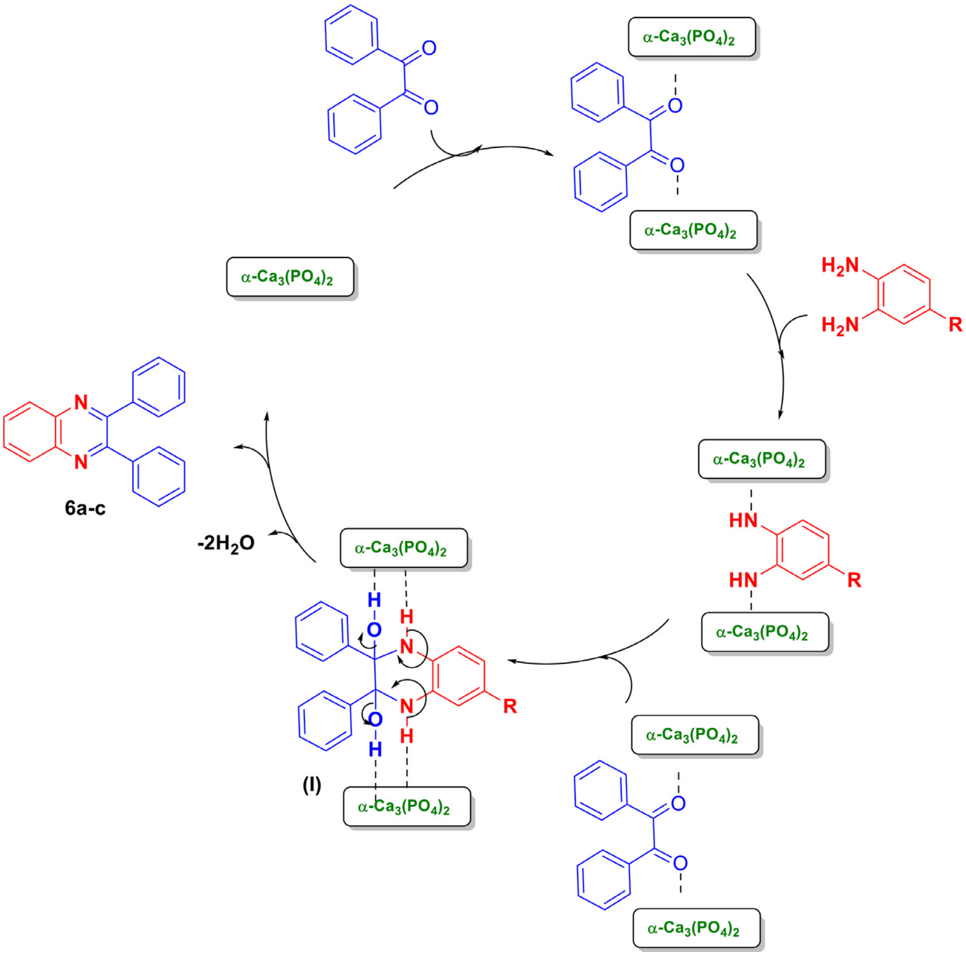
The α-$Ca_3(PO_4)_2$ is prepared and characterized successfully. Then, we studied their catalytic performance in the Knoevenagel condensation and the synthesis of 2,3-diphenylquinoxaline. We performed the condensation of p-chlorobenzaldehyde **1a**, and the malononitrile **2a** in 2 ml of ethanol at room temperature as model reaction (Scheme 1). Similarly, we accomplished the synthesis of 2,3-diphenylquinoxaline via condensation between the o-phenylenediamine **4a** with the benzile **5a** (Scheme 2) in 2 ml of EtOH at room temperature.

This reaction is considered a model reaction. The results are grouped in Table 2. The results show that in the absence of the catalyst product **3a** is obtained with a yield of 54% after 60 min (Table 2, **Entry 1**) and product **6a** with a yield of 47% for 10 min (Table 2, **Entry 1**). On the other hand, both reactions are performed in the presence of catalyst leads to the desired product **3a** with a yield of 91% during 30 min of agitation (Table 2, **Entry 2**) and provides the desired product **6a** after 10 min of agitation with a very



Scheme 5. Suggested transformation mechanism for the synthesis of alkenes catalyzed by α-Ca_3 $(PO_4)_2$.

good yield (Table 2, **Entry 2**). This showed clearly that our catalyst exhibits significant catalytic activity in both reactions. To choose the most suitable solvent for the preparation of products **3a** and **6a**. We have carried out model reactions in different solvents. The results are represented in Table 3. According to Table 2, the synthesis of products **3a** and **6a** in protic polar solvents (MeOH and EtOH) with excellent yields (Table 3, **Entry 1**). On the other hand, the reaction in the apolar solvent (THF) allows the product **3a** to be obtained with a good performance for 45 min (Table 3, **Entry 2**). For the aprotic polar solvent such as acetonitrile, the desired product **3a** is obtained with a moderate yield for 40 min (Table 3, **Entry 3**). Therefore, ethanol is chosen as an adequate ecological solvent for both moderate point-of-view performance reactions and very short time. To study the effect of α-$Ca_3(PO_4)_2$ mass on the performance of products **3a** and **6a**. We performed model condensation by varying the amount of our catalyst from 0.5 to 20 mg in the operating conditions described above. The results are reported in the Table 4. The obtained results showed that a catalytic quantity of 8 mol%/2.56 mg was sufficient to give very good yields for the formation of products **3a** and **6a** (Table 4, **Entry 8**). When you exceed the optimum mass, the yields remain almost constant (Table 4, **Entries 9 and 10**). But for the mass of 20 mol%/6.44 mg there is a slight decrease in yield (Table 4, **Entry 11**). Therefore, this decrease in the α-$Ca_3(PO_4)_2$ mass has a slight influence on the yields of products **3a** and **6a**. This results can be explained by the decrease in α-$Ca_3(PO_4)_2$ in reactions which can influence the interaction between substrates and our catalyst. Finally, we found that the best results are obtained when the formation of products **3a** and **6a** is carried out in the presence of 8 mol%/2.56 mg of α-$Ca_3(PO_4)_2$ in 2 mL of ethanol at room temperature. The optimal reaction conditions were subsequently applied in the generalization of Knoevenagel condensation using substituted aromatic aldehydes and malononitrile, ethyl cyanoacetate and methyl cyanoacetate. The results are listed in Table 5. Based on the present results, we have noticed that the condensation of aromatic aldehydes with malononitrile has resulted in the desired products **(3a–d)** with good yields **(91–96%)** in very short times. The same remark is made when malononitrile is replaced with methyl cyanoacetate or ethyl cyanoacetate **(3e–l)**. Certainly, the desired products are also obtained with good yields that are varied between **83 and 94%** in processing times greater than 30 min which is reflected in the fact that methyl cyanoacetate or ethyl cyanoacetate is less reactive than malononitrile. According to the present results, it can be inferred that the substitutes nature of the aldehyde level has no influence on yields and processing times. After optimizing the conditions of the model reaction on the **6a** product formation, this process was generalized for the synthesis of series of 2.3-diphenylquinoxalines derivatives. Indeed, the reaction was achieved from the condensation of various o-phenylenediamine substituted **4** with benzile **2**. The results are listed in Table 6. Based on the results represented in Table 6, we found that optimal conditions remaining still effective for the synthesis of 2.3-diphenylquinoxaline drifts. In addition, the desired products are obtained with good to excellent yields in front the shorter reaction times regardless of the nature of the 1.2-diamine substitutions (**Product 6a–c**). The catalyst efficiency depends also on its long durability, i.e. the possibility of being reused without any significant loss of catalytic activity even after several cycles of use. To do this, the reuse of α-$Ca_3(PO_4)_2$ stud-



Scheme 6. Proposed transformation mechanism for the synthesis of 2,3-diphenylquinoxaline derivatives in the presence of α-Ca_3 $(PO_4)_2$.

ied was carried out under optimal conditions for product formation **3a** (Scheme 3) and **6a** (Scheme 4). The catalyst removed from the reaction mixture by simple filtration was thoroughly washed with ethanol and dried at 80 °C. The recycled catalyst can be used for subsequent reactions without loss of catalytic activity. The results are grouped in Fig. 6. The results show clearly that the catalyst α-$Ca_3(PO_4)_2$ could be recycled five times in a run without any significant loss of catalytic activity (Fig. 6). According to our knowledge, the reuse of this catalyst is significantly superior to most catalysts reported in the literature. The experimental studies conducted during this work were accompanied by a comparative study between the efficacy of α-$Ca_3(PO_4)_2$ and those of other announced catalysts dabs the literature regarding knoevenagel condensation and the synthesis of 2.3-diphenylquinoxaline. The results are grouped in Table 7. From the table results, it can be concluded that heterogeneous catalyst α-$Ca_3(PO_4)_2$ has a very interesting catalytic activity compared to other catalysts. Moreover, the procedure described remains remarkable and comparable to other methods in terms of mild conditions, very short reaction times, excellent yields and the amount of catalyst used. For a better understanding the role played by the present catalyst in the activation of substrates. An alkene formation mechanism in the presence of α-$Ca_3(PO_4)_2$ was proposed and illustrated in Scheme 5. First, aldehyde is active by coordinating the oxygen free doublet with the calcium of the catalyst α-$Ca_3(PO_4)_2$. Then, the basic sites of PO_4^{3-} activate the acid protons of the active methylene compounds in the form of a carbanion. The latter with active aldehyde leads to the formation of the Carbon-Carbone Bond (**I**). Followed intramolecular dehydration to finally get the desired products **3a-l**. The proposed catalytic mechanism for the synthesis of 2.3-diphenylquinoxalins derivatives in the presence of α-$Ca_3(PO_4)_2$ is shown in Scheme 6. Initially, the electrophilic sites of catalyst α-$Ca_3(PO_4)_2$ activated the carbonyl functions of Benzil and the two amine functions of orthophenylenediamine. The latter two are activated to facilitate the nucleophile attack of diamine grouping of the orthophenylenediamine on the benzil activated to form the intermediate (**I**). Finally, we have two intramolecular nucleophile attacks followed by elimination of two molecules of H_2O to give the desired products **6a–c**.

4. Conclusion

In the present manuscript, we have prepared a solid structure α-$Ca_3(PO_4)_2$ which subsequently identified by different analysis technique. In order to study the catalytic performance of our catalytic support in Knoevenagel condensation and the synthesis of 2.3-diphenylquinoxalines drifts under sustainable conditions. The obtained results showed that α-$Ca_3(PO_4)_2$ possessed an interesting catalytic activity in a more ecological environment (2 mL Ethanol) at room temperature. These methodologies have several advantages including, very short reaction times (2.3-diphenylquinoxalines 10–12 min and Knoevenagel condensation 30–60 min), excellent yields, (2.3-diphenylquinoxalines 90–98% and Knoevenagel condensation 83–96%), use of a small quantity of catalyst, ease recovery and reuse of α-$Ca_3(PO_4)_2$ that can be recycled instantly more than five times without significant loss of their catalytic performance. Furthermore, α-$Ca_3(PO_4)_2$ shows an excellent catalytic activity for the synthesis of organic compounds with biological activity, compared to more expensive and environmentally harmful homogeneous catalysts.

Contribution author statement

Haddou Anahmadi and Zakaria Benzekri performed the synthesis and characterization and writ-up of the manuscript. Majda Fathi performed the synthesis and characterization. Fatima El hajri and Sarra Sibous performed part of the manuscript. Said Boukhris, Brahim Chafik El Idrissi, Mohamed Salahdine El youbi and Abdelaziz Souizi designed the work and were part of the manuscript writ-up.

Declaration of Competing Interest

The authors of this manuscript report that there are no conflicts of interest relevant to this research work.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.molstruc.2021.131449.

References

[1] Z. Amjad, Calcium phosphates in biological and industrial systems, Kluwer Academic Publishers, USA, 1997.

[2] J.P. Budin, J.C. Michel, F. Auzel, Oscillator strengths and laser effect in $Na_2Nd_2Pb_6$ (PO_4) $6C_{l2}$ (chloroapatite), a new high-Nd-concentration laser material, J. Appl. Phys. 50 (2) (1979) 641–646.

[3] A.O. Wright, M.D. Seltzer, J.B. Gruber, B.H. Chai, Site-selective spectroscopy and determination of energy levels in Eu^{3+}-doped strontium fluorophosphate, J. Appl. Phys. 78 (4) (1995) 2456–2467.

[4] M. Gorbunoff, The interaction of proteins with hydroxyapatite: I. Role of protein charge and structure, J. Anal. Biochem. 136 (2) (1984) 425–432.

[5] Y.O.I.C.H.I. Shibusawa, N.A.O.K.O. Miwa, T.O.H.R.U. Hirashima, U.S.H.I.H.O Matsumoto, Separation of low density and very low density lipoproteins from human serum by hydroxyapatite chromatography, J. Liq. Chromatogr. Relat. Technol. 17 (6) (1994) 1203–1217. doi:10.1080/10826079408013756.

[6] Legeros, R. Z. In Calcium phosphates in oral biology and medicine, in "Monographs in oral Science" Ed. Myers H.M., Karger, London, 1991, 15, 172–201.

[7] H. Aoki, Medical applications of hydroxyapatite, Ishiyaku Euro America, Inc., Tokyo, 1994.

[8] M.P. Ginebra, T. Traykova, J. Planell, Calcium phosphate cements: Competitive drug carriers for the musculoskeletal system? Biomaterials 27 (10) (2006) 2171–2177.

[9] Tadier S., "Etude des propriétés physico-chimiques et biologiques de ciments biomédicaux à bas de carbonate de calcium: apport de procédé de coboyage", Thèse de Doctorat, INP, Toulouse, 2009.

[10] S. Sibous, T. Ghailane, S. Houda, R. Ghailane, S. Boukhris, A. Souizi, Green and efficient method for the synthesis of 1, 5-benzodiazipines using phosphate fertilizers as catalysts under free solvent, Med. J. Chem. 6 (3) (2017) 53–59.

[11] (a) S. Sibous, S. Boukhris, R. Ghailane, N. Habbadi, A. Hassikou, A. Souizi, Easy synthesis of 3, 4-dihydropyrimidin-2-(1H)-ones using phosphate fertilizers MAP, DAP And TSP as efficient catalysts, J. Turkish Chem. Soc. Sect. Chem. 4 (2) (2017) 477–488; (b) Z. Benzekri, S. Sibous, H. Serrar, A. Ouasri, S. Boukhris, R. Ghailane, A. Souizi, NH_3 $(CH_2)_5NH_3BiCl_5$ as a new hybrid and efficient catalyst for the synthesis of 1-(benzothiazolylamino) methyl-2-naphthol derivatives under solvent-free conditions, J. Mol. Struct. 1202 (2020) 127308.

[12] Y. Merroun, S. Chehab, T. Ghailane, M. Akhazzane, A. Souizi, R. Ghailane, Preparation of tin-modified mono-ammonium phosphate fertilizer and its application as heterogeneous catalyst in the benzimidazoles and benzothiazoles synthesis, React. Kinet. Mech. Catal. 126 (1) (2019) 249–264.

[13] Z. Benzekri, K. El Mejdoubi, S. Boukhris, B. Sallek, B. Lakhrissi, A Souizi, Dicalcium phosphate dehydrate DCPD as a highly efficient and reusable catalyst for Knoevenagel condensation, Synth. Commun. 46 (5) (2016) 442–451.

[14] E. Knoevenagel, Mittheilungen Ueber eine Darstellungsweise der Glutarsäure, Ber. Dtsch. Chem. Ges. 27 (1894) 2337–2347.

[15] E. Knoevenagel, Ueber eine darstellungsweise des benzylidenacetessigesters, Ber. Dtsch. Chem. Ges. 29 (1896) 172–174.

[16] S. Sebti, A. Saber, A. Rhihil, Phosphate naturel et phosphate trisodique: nouveaux catalyseurs solides de la condensation de Knoevenagel en Milieu Hétérogène, Tetrahedron Lett. 35 (1994) 9399–9400.

[17] S. Sebti, A. Smahi, A. Solhy, Natural phosphate doped with potassium fluoride and modified with sodium nitrate: efficient catalysts for the Knoevenagel condensation, Tetrahedron Lett. 43 (2002) 1813–1815.

[18] B. Xu, Q. Xu, X. Han, X. Ma, J. Wang, T. Kannan, J. Niu, Polyoxomolybdates as efficient catalysts for Knoevenagel condensation reaction of benzaldehyde and ethyl cyanoacetate under mild condition, J. Mater. Sci. 56 (7) (2021) 4654–4665.

[19] J.N. Appaturi, T. Pulingam, R.J. Ramalingam, F. Khoerunnisa, T.C. Ling, S.H. Tan, E.P. Ng, Acid-base bifunctional SBA-15 as an active and selective catalyst for synthesis of ethyl α-cyanocinnamate via Knoevenagel condensation, Microporous Mesoporous Mater (2021) 111091, doi:10.1016/j.micromeso.2021.111091.

[20] H. El Aadad, Z. Benzekri, S. Boukhris, A. Chahine, Synthesis, characterization of polystyrene-phosphate films and their application as heterogeneous catalyst for Knoevenagel condensation in solvent-free conditions, J. Chem. Sci. 132 (1) (2020) 1–13.

[21] J.P. Grass, K. Klühspies, B. Reiprich, W. Schwieger, A. Inayat, Layer-Like Zeolite X as Catalyst in a Knoevenagel Condensation: The Effect of Different Preparation Pathways and Cation Exchange, Catalysts 11 (4) (2021) 474.

[22] K.B. Badiger, K Kamanna, Knoevenagel condensation reaction catalysed by agro-waste extract as a greener solvent catalyst, Org. Commun. 14 (1) (2021) 91.

[23] A. Sharma, R. Dixit, S. Sharma, S. Dutta, S. Yadav, B. Arora, R.K. Sharma, Efficient and sustainable Co3O4 nanocages based nickel catalyst: A suitable platform for the synthesis of quinoxaline derivatives, Mol. Catal. 504 (2021) 111454.

[24] D. Sindhuja, M. Gopiraman, P. Vasanthakumar, N. Bhuvanesh, R. Karvembu, Ruthenium− p− cymene complexes with acylthiourea, and its heterogenized form on graphene oxide act as catalysts for the synthesis of quinoxaline derivatives, J. Organomet. Chem. 949 (2021) 121933, doi:10.1016/j.jorganchem.2021.121933.

[25] K.J. Tamuli, S. Nath, M. Bordoloi, In water organic synthesis: Introducing itaconic acid as a recyclable acidic promoter for efficient and scalable synthesis of quinoxaline derivatives at room temperature, J. Heterocycl. Chem. 58 (4) (2021) 983–1002.

[26] R.B. Baudy, L.P. Greenblatt, I.L. Jirkovsky, M. Conklin, R.J. Russo, D.R. Bramlett, DM. Kowal, Potent quinoxaline-spaced phosphono. alpha.-amino acids of the AP-6 type as competitive NMDA antagonists: synthesis and biological evaluation, J. Med. Chem. 36 (3) (1993) 331–342.

[27] S.B. Lee, Y.I. Park, M.S. Dong, Y.D. Gong, Identification of 2, 3, 6-trisubstituted quinoxaline derivatives as a Wnt2/β-catenin pathway inhibitor in non-small–cell lung cancer cell lines, Chem. Lett. 20 (19) (2010) 5900–5904.

[28] M.M. Badran, K.A. Abouzid, M.H.M Hussein, Synthesis of certain substituted quinoxalines as antimicrobial agents (part II), Arch. Pharm. Res. 26 (2) (2003) 107–113.

[29] H. Zheng, C. Jiang, M.H. Chiu, J.M. Covey, K.K Chan, Chiral pharmacokinetics and inversion of enantiomers of a new quinoxaline topoisomerase IIβ poison in the rat, Drug Metab. Dispos 30 (3) (2002) 344–348.

[30] H. Cerecetto, E. Dias, R. Di Maio, M. González, S. Pacce, P. Saenz, M. Lema, Synthesis and herbicidal activity of N-oxide derivatives, J. Agric. Food Chem. 48 (7) (2000) 2995–3002.

[31] C.W. Lindsley, Z. Zhao, W.H. Leister, R.G. Robinson, S.F. Barnett, D. Defeo-Jones, M.E. Duggan, Allosteric Akt (PKB) inhibitors: discovery and SAR of isozyme selective inhibitors, Chem. Lett. 15 (3) (2005) 761–764.

[32] M. Loriga, S. Piras, P. Sanna, G. Paglietti, Quinoxaline chemistry. Part 7. 2-[aminobenzoates]-and 2-[aminobenzoylglutamate]-quinoxalines as classical antifolate agents. Synthesis and evaluation of in vitro anticancer, anti-HIV and antifungal activity, Farmaco 52 (3) (1997) 157–166.

[33] L.E. Seitz, W.J. Suling, R.C Reynolds, Synthesis and antimycobacterial activity of pyrazine and quinoxaline derivatives, J. Med. Chem. 45 (25) (2002) 5604–5606.

[34] W. He, M.R. Myers, B. Hanney, A.P. Spada, G. Bilder, H. Galzcinski, M.H. Perrone, Potent quinoxaline-Based inhibitors of PDGF receptor tyrosine kinase activity. Part 2: the synthesis and biological activities of RPR127963 an orally bioavailable inhibitor, Bioorganic Med.Chem. Lett. 13 (18) (2003) 3097–3100.

[35] E.A. Fayed, Y.A. Ammar, M.A. Saleh, A.H. Bayoumi, A. Belal, A.B. Mehany, A. Ragab, Design, synthesis, antiproliferative evaluation, and molecular docking study of new quinoxaline derivatives as apoptotic inducers and EGFR inhibitors, J. Mol. Struct. 1236 (2021) 130317.

[36] Y.B. Kim, Y.H. Kim, J.Y Park, S.K Kim, Synthesis and biological activity of new quinoxaline antibiotics of echinomycin analogues, Bioorganic Med. Chem. Lett. 14 (2) (2004) 541–544.

[37] J.P. Duan, P.P. Sun, C.H Cheng, New iridium complexes as highly efficient Orange–Red emitters in organic Light-Emitting diodes, Adv. Mater 15 (3) (2003) 224–228.

[38] D. Schneidenbach, S. Ammermann, M. Debeaux, A. Freund, M. Zöllner, C. Daniliuc, H.H Johannes, Efficient and long-time stable red iridium (III) complexes for organic light-emitting diodes based on quinoxaline ligands, Inorg Chem. 49 (2) (2009) 397–406.

[39] M. Ouakki, M. Galai, Z. Benzekri, C. Verma, E. Ech-chihbi, S.A.V.A.Ş Kaya, M. Cherkaoui, Insights into corrosion inhibition mechanism of mild steel in 1 M HCl solution by quinoxaline derivatives: electrochemical, SEM/EDAX, UV-visible, FT-IR and theoretical approaches, Colloids Surf. A Physicochem. Eng. Asp. 611 (2021) 125810.

[40] G. Kaur, A. Singh, N. Kaur, B. Banerjee, A general method for the synthesis of structurally diverse quinoxalines and pyrido-pyrazine derivatives using camphor sulfonic acid as an efficient organo-catalyst at room temperature, Synth. Commun. 51 (7) (2021) 1121–1131.

[41] S. Sajjadifar, I. Amini, M. Karimian, Synthesis and Characterization of Fe$_3$O$_4$@ APTES@ MOF-199 Magnetic Nanocatalyst and Its Application in the Synthesis of Quinoxaline Derivatives. Iran, J. Catal. 11 (1) (2021) 59–67.

[42] S. Sajjadifar, I. Amini, G. Mansouri, S. Alimohammadi, Fe$_3$O$_4$@ APTES@ isatin-SO$_3$H as heterogeneous and efficient catalyst for the synthesis of quinoxaline derivatives, Eurasian Chem. Commun. 2 (5) (2020) 626–633.

[43] D. Sarma, B. Majumdar, B. Deori, S. Jain, TK. Sarma, Photoinduced Enhanced Decomposition of TBHP: A Convenient and Greener Pathway for Aqueous Domino Synthesis of Quinazolinones and Quinoxalines, ACS omega 6 (18) (2021) 11902–11910.

[44] A. Kamal, K.S. Babu, S.A. Hussaini, R. Mahesh, A. Alarifi, Amberlite IR-120H, an efficient and recyclable solid phase catalyst for the synthesis of quinoxalines: a greener approach, Tetrahedron Lett. 56 (21) (2015) 2803–2808.

[45] R.G. Carrodeguas, & De Aza, S. α-Tricalcium phosphate: Synthesis, properties and biomedical applications, Acta Biomater 7 (10) (2011) 3536–3546.

[46] J. Czechowska, A. Zima, D. Siek, A. Ślósarczyk, Influence of sodium alginate and methylcellulose on hydrolysis and physicochemical properties of α-TCP based materials, Ceram. Int. 44 (6) (2018) 6533–6540.

[47] J. Czechowska, A. Zima, Z. Paszkiewicz, J. Lis, A. Ślósarczyk, Physicochemical properties and biomimetic behaviour of α-TCP-chitosan based materials, Ceram. Int. 40 (4) (2014) 5523–5532.

[48] J. Mondal, A. Modak, A Bhaumik, Highly efficient mesoporous base catalyzed Knoevenagel condensation of different aromatic aldehydes with malononitrile and subsequent noncatalytic Diels–Alder reactions, J. Mol. Catal. A Chem. 335 (1) (2011) 236–241.

[49] Y. Zhang, Y. Zhao, C. Xia, Basic ionic liquids supported on hydroxyapatite-encapsulated γ-Fe$_2$O$_3$ nanocrystallites: An efficient magnetic and recyclable heterogeneous catalyst for aqueous Knoevenagel condensation, J. Mol. Catal. A: Chem. 306 (1) (2009) 107–112.

[50] F. Su, M. Antonietti, X. Wang, mpg-C 3 N 4 as a solid base catalyst for Knoevenagel condensations and transesterification reactions, Catal. Sci. Technol. 2 (5) (2012) 1005–1009.

[51] S. Zhao, Y. Chen, Y.F. Song, Tri-lacunary polyoxometalates of Na8H [PW9O34] as heterogeneous Lewis base catalysts for Knoevenagel condensation, cyanosilylation and the synthesis of benzoxazole derivatives, Appl. Catal. 475 (2014) 140–146.

[52] Z. Benzekri, H. El Aadad, S. Sibous, H. Serrar, S. Boukhris, A. Chahine, A. Souizi, Improvement of the catalytic performance of hybrid nanocomposite based on phosphate-benzimidazole in Knoevenagel condensation, Heliyon 6 (11) (2020) e05293.

[53] F. El hajri, Z. Benzekri, S. Sibous, A. Ouasri, S. Boukhris, A. Hassikou, A. Rhandour, A. Souizi, Bis [hydrazinium (1$^+$)] hexafluoridosilicate:(N$_2$H$_5$)$_2$SiF$_6$ novel hybrid crystal as an efficient, reusable and environmentally friendly heterogeneous catalyst for Knoevenagel condensation and synthesis of biscoumarin derivatives, J. Mol. Struct. 1230 (2021) 129890.

[54] M. Jafarpour, A. Rezaeifard, A zirconium Schiff base complex immobilized on starch-coated maghemite nanoparticles catalyzes heterogeneous condensation of 1, 2-diamines with 1, 2-dicarbonyl compounds, Transition Met. Chem. 41 (2) (2016) 205–211.

[55] M. Shamsi-Sani, F. Shirini, M.Seddighi Abedini, M Synthesis of benzimidazole and quinoxaline derivatives using reusable sulfonated rice husk ash (RHA-SO$_3$H) as a green and efficient solid acid catalyst, Res. Chem. Intermed. 42 (2) (2016) 1091–1099.

[56] N. Thimmaraju, S.M. Shamshuddin, Synthesis of 2,4,5-trisubstituted imidazoles, quinoxalines and 1,5-benzodiazepines over an eco-friendly and highly efficient ZrO$_2$–Al$_2$O$_3$ catalyst, RSC Adv. 6 (65) (2016) 60231–60243.

[57] F. Rajabi, D. Alves, R Luque, An Efficient and Recyclable Nanoparticle-Supported Cobalt Catalyst for Quinoxaline Synthesis, Molecules 20 (11) (2015) 20709–20718.

[58] S. Chehab, Y. Merroun, T. Ghailane, N. Habbadi, S. Boukhris, A. Hassikou, M. Akhazzane, A. Kerbal, R. Ghailane, A. Daich, A. Souizi, A new process for Na$_2$Ca(HPO$_4$)$_2$ synthesis and its application as a heterogeneous catalyst in Knoevenagel condensation, Mediterr. J. Chem. 7 (1) (2018) 56–67.

[59] B. Malek, I. Bahammou, O. Zimou, A. El Hallaoui, R. Ghailane, S. Boukhris, A. Souizi, Eco-friendly synthesis of quinoxaline derivatives using mineral fertilizers as heterogeneous catalysts, J. Turk. Chem. Soc. A: Chem. 7 (2) (2020) 427–440.